BOOK OF ABSTRACTS

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WBC2016

10th World Biomaterials Congress
May 17-22, 2016 | Montréal, Canada

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ML-SM-050, Rev. 1

P.0777

Influence of mesh structure on surgical healing in abdominal wall hernia repair

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Synthetic surgical mesh has become an important tool in the armamentarium of the surgeon reconstructing soft tissue defects and hernias. Mechanical failure and recurrence remain primary causes of repair revision and mesh removal in hernia repair[5]-[30]. This study evaluated the qualitative and quantitative morphology of intramesh fibrous connective tissue (FCT) healing in a range of clinically used knitted (polypropylene and polyester) and non-woven (polypropylene) barrier and non-barrier surgical meshes implanted in a rabbit model.

The results demonstrated that the knitted mesh displayed intramesh FCT healing that was concentric to the mesh fibers[27] with significant between fiber FCT discontinuities due to the presence of adipose tissue. Non-woven surgical mesh resulted in a more linearly oriented intramesh FCT healing, primarily parallel to the plane of the non-woven mesh, with minimal FCT discontinuity.

Non-woven surgical mesh had a significantly reduced incidence of FCT discontinuity and a higher probability of a FCT response than knitted surgical mesh.

The presence of significant discontinuities in intramesh FCT healing in this study, especially in lightweight knitted surgical mesh which has been associated with mechanical failures clinically[16],[17], underscores the importance of complete FCT healing for secure long term hernia repair. In conclusion, non-woven monofilament constructions of barrier and non-barrier surgical mesh resulted in highly congruent intramesh FCT healing when compared to commonly used barrier and non-barrier knitted surgical mesh constructions which demonstrated significant FCT healing discontinuities.

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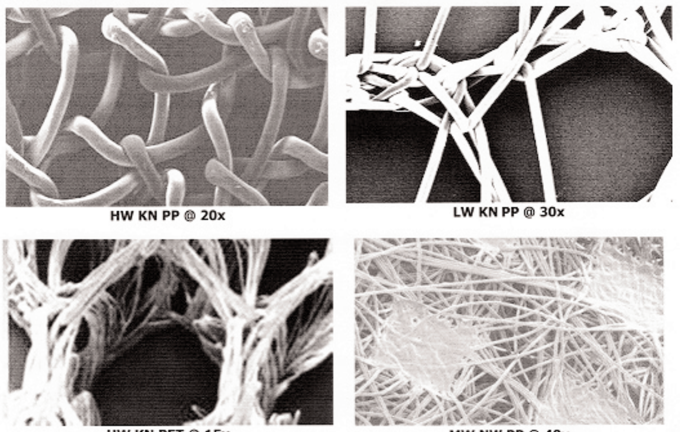

Figure 1: Overview of knitted and non-woven non-barrier surgical mesh structures at various magnifications.

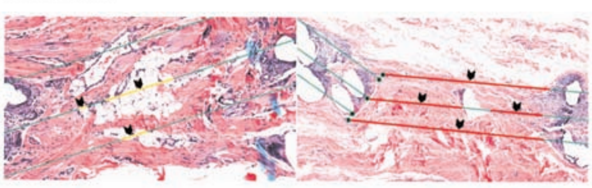

Figure 2: (a) H&E image displaying the 10-50-90 wound length measurement lines (green) and its overlaid fatty infiltrate (yellow) measurement at 15x. (b) H&E image at 10x displaying similar overlaid measurement lines but for no response tissue (red).

Surgical Mesh Category	N	Ave Adipose Tissue Response	Max Adipose Tissue Response	Ave Occurrence Adipose Tissue Response
Non-barrier Mesh				
LW KN PP I	75	18.9%	84.2%	50.7%
LW KN PP II	55	10.9%	92.5%	40.0%
HW KN PP	33	13.0%	49.5%	69.7%
HW KN PET	55	8.0%	57.8%	43.6%
WM NW PP	66	0.2%	13.8%	4.5%
Barrier Mesh*				
MW KN PP/Omega 3	66	8.0%	62.7%	36.4%
MW KN PP/ORC	105	8.0%	67.9%	29.5%
HW KN PET/collagen	39	6.4%	58.5%	38.5%
MW NW PP/silicone	87	1.4%	28.1%	8.0%
Mesh Type				
Non-barrier mesh	284	10.3%	13.8% - 92.5%	4.5% - 68.7%
Barrier Mesh	297	5.9%	28.1% - 67.9%	8.0% - 38.5%
Mesh Construction				
Knitted - KN	428	10.6%	49.5% - 92.5%	29.5% - 69.7%
Non-woven - NW	153	1.0%	13.8% - 28.1%	4.5% - 8.0%

* Non-barrier mesh base construction/barrier material

The presence of significant discontinuities in intramesh FCT healing in this study, especially in lightweight knitted surgical mesh which has been associated with mechanical failures clinically[16],[17], underscores the importance of complete FCT healing for secure long term hernia repair. In conclusion, non-woven monofilament constructions of barrier and non-bar surgical mesh resulted in highly congruent intramesh FCT healing when compared to commonly used barrier and non-barrier knitted surgical mesh constructions which demonstratec significant FCT healing discontinuities.

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ML-SM-50, Rev. 1

Influence of Mesh Structure on Surgical Healing In Abdominal Wall Hernia Repair

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Synthetic surgical mesh has become an important tool in the armamentarium of the surgeon reconstructing soft tissue defects and hernias. Mechanical failure and recurrence remain primary causes of repair revision and mesh removal in hernia repair. This study evaluated the qualitative and quantitative morphology of intramesh fibrous connective tissue (FCT) healing in a range of clinically used knitted (polypropylene and polyester) and non-woven (polypropylene) barrier and non-barrier surgical meshes implanted in a rabbit model. The results demonstrated that the knitted mesh displayed intramesh FCT healing that was concentric to the mesh fibers with significant between fiber FCT discontinuities. Non-woven surgical mesh resulted in a more linearly oriented intramesh FCT healing, primarily parallel to the plane of the non-woven mesh, with minimal FCT discontinuity. Non-woven surgical mesh had a significantly higher probability of FCT response without discontinuity than knitted surgical mesh. The presence of significant discontinuities in intramesh FCT healing in this study, especially in lightweight knitted surgical mesh which has been associated with mechanical failures clinically, underscores the importance of complete FCT healing for secure long term hernia repair. In conclusion, non-woven monofilament constructions of barrier and non-barrier surgical mesh resulted in highly congruent intramesh FCT healing when compared to commonly used barrier and non-barrier knitted surgical mesh constructions which demonstrated significant FCT healing discontinuities.

1. Introduction

The repair of inguinal and ventral hernias is a continuing challenge for surgeons. The use of surgical mesh has increased [1] and positively impacted the treatment of primary hernias by reducing 3 year recurrence rates to low levels in inguinal – 7% to 1% - [2] and ventral – 43% to 24% - [3] open hernia repair. Laparoscopic hernia repair with surgical mesh has led to further reduction in recurrence rates especially for ventral hernia repair with large, multi-center series reporting recurrence rates less than 5% [4]. Associated with this broader clinical use of especially heavier weight (HW) knitted surgical meshes, new clinical failure modes related to the tissue healing properties of the surgical meshes have resulted. Hernia repairs have been reported to be impacted by problems with infection, mechanical mesh failure, hernia recurrence, mesh migration, repair site pain, excessive tissue reaction, intestinal obstruction, adhesions, seroma and erosion that can lead to fistula formation [5, 6].

In an attempt to address some of these problems, an ever expanding plethora of lighter weight (LW) knitted surgical meshes have been developed to improve upon the performance of their original heavy weight counterparts. These lighter weight meshes have achieved their reduced weight by pore size increase (wider fiber spacing) and/or fiber diameter reduction [7], both of which increase their compliance [8] but reduce their strength [9, 10]. Although modified in weight per unit area, these lighter weight knitted configurations are still composed of the same biocompatible polypropylene (PP) polymers and use the same knitting technology of their heavy weight counterparts. Early investigations proposed that although these lighter weight knitted meshes had lower overall strength, they were adequate for full thickness abdominal wall hernia reconstructions including the bridging of defects [11] as their strength exceeded 16 N/cm [4]. The changes to pore size and fiber diameter, by reducing the total amount of synthetic material implanted, altered the tissue reaction and incorporation properties of the lighter weight meshes [9].

With the advent of lighter weight knitted surgical meshes, success in reducing discomfort, pain, shrinkage and excessive fibrosis has been demonstrated [12-15]. Unfortunately, this lighter weight mesh concept has been associated with central mesh failures and increased recurrence in full thickness abdominal wall repairs [16-18]. The purpose of this study was to compare the healing properties of lighter weight and heavyweight knitted surgical mesh configurations to a mid-weight random matrix of non-woven, monofilament polypropylene microfibers heat bonded together (MW NW PP) to form a surgical mesh. It is hypothesized that the random, microfiber nature of this non-woven matrix will lead to a more complete fibrous connective tissue response throughout the surgical mesh for improved hernia defect reinforcement. In this way the benefits of a lighter weight mesh could be fully realized and the occurrence of central mesh failure noted with knitted constructions potentially eliminated. If achieved, this would come closer to the ideal of using a synthetic mesh to reinforce the poor fascial strength [19] in hernia patients without negatively affecting the physiologic functioning of the abdominal wall or inadequately strengthening the abdominal wall in full thickness defects.

2. Materials and methods

2.1 Test Configuration

The tested configurations in this study included clinically available non-barrier and barrier surgical meshes based upon knitted and non-woven technologies representing a range of mesh weights and pore structures as detailed in Table 1 and Figure 1.

Table 1: Experimental groups utilized in the study

Surgical Mesh	Structure	Fiber Type	Fiber Material	Implant N=	Mesh Wt.	Designation (mesh/barrier)
Non-barrier	Knitted	Monofilament	Polypropylene	4	102 g/m^2	HW KN PP
	Knitted	Multifilament	Polyester	8	119 g/m^2	HW KN PET
	Knitted	Monofilament	Polypropylene	8	41 g/m^2	LW KN PP I
	Knitted	Monofilament	Polypropylene	8	28 g/m^2	LW KN PP II
	Non-woven	Monofilament	Polypropylene	8	80 g/m^2	MW NW PP
Barrier	Knitted	Multifilament	Polyester	8	156 g/m^2	HW KN PET/collagen gel
	Knitted	Monofilament	Polypropylene	8	321 g/m^2	MW KN PP/Omega 3 gel
	Knitted	Monofilament	Polypropylene	8	190 g/m^2	MW KN PP/ORC
	Non-woven	Monofilament	Polypropylene	8	350 g/m^2	MW NW PP/silicone

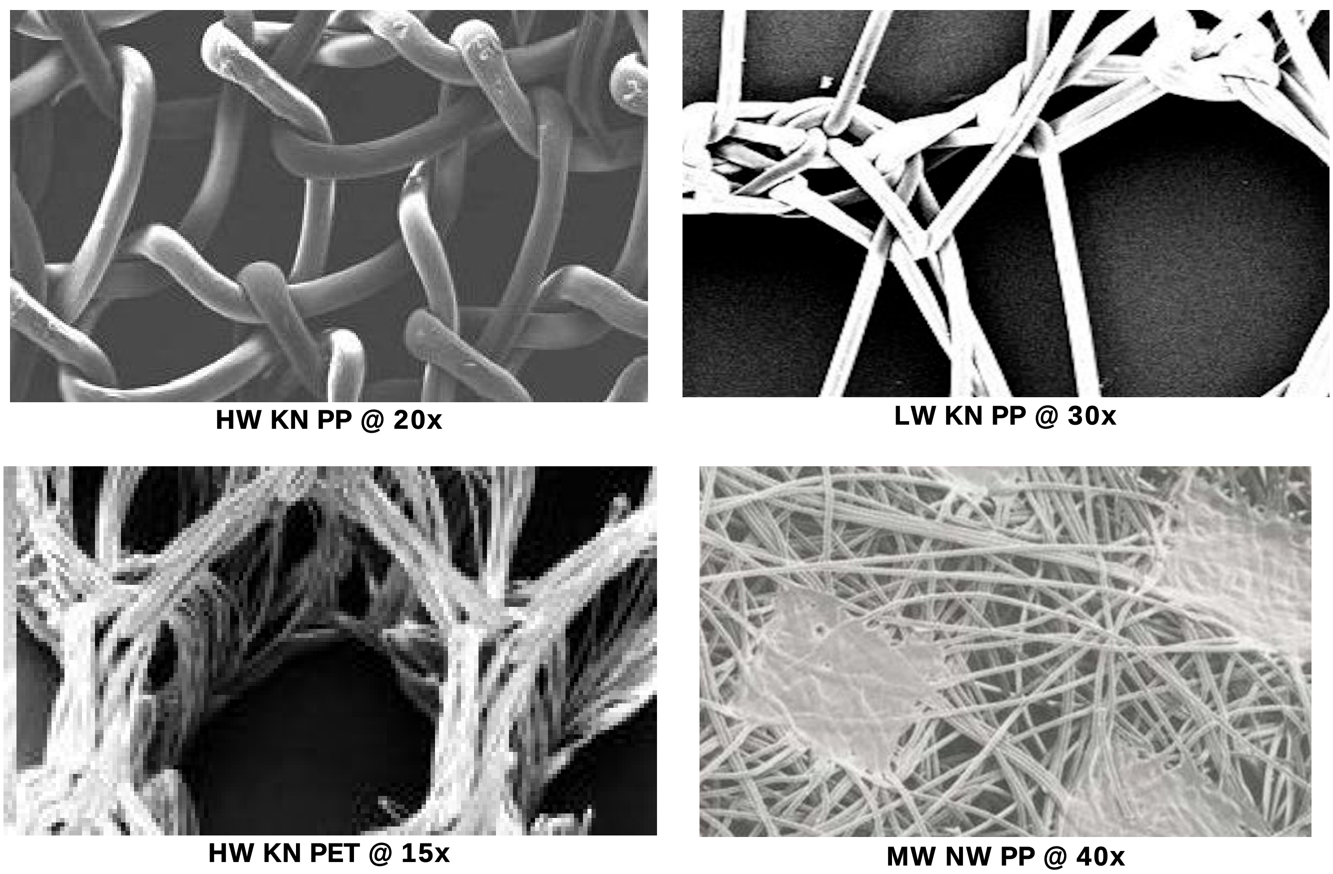


Figure 1: Overview of knitted and non-woven non-barrier surgical mesh structures at various magnifications.

2.2 Implantation, Retrieval , and Histology

Sixty eight (68) 4 cm squares of non-barrier and barrier surgical mesh were implanted in seventeen (17) New Zealand white rabbits, anterior (non-barrier mesh) and posterior (barrier mesh) to the abdominal wall. The distribution of each mesh type implanted is shown in Table 1. Four squares of the same type of surgical mesh were implanted in each rabbit symmetrically to the midline and between thoracic and pelvic borders of the abdominal wall for 180 days, maximizing the separation between all the implants. Each 4 cm square implant was fixated at the corners using 3-0 Prolene and mid edge using Dermabond tissue adhesive. Animals were housed in conditions of constant light and temperature receiving food and water *ad libidum*. The study was approved by the Dartmouth Hitchcock Medical Center Institutional Animal Care and Use Committee (IACUC) and conducted in accordance with federal Association for Assessment and Accreditation of Laboratory Animal Care (AALAC) research guidelines.

At retrieval all surgical mesh implants were excised enbloc with a minimum border of 1 cm of abdominal wall musculofascial tissue on the perimeter of the specimen. Each healed surgical mesh specimen was cooled for stability during cutting and four evenly distributed 2 cm long thin strips with attached abdominal wall were cut for histopathologic analysis. The cut thin strips from each healed surgical mesh implant were placed in histological processing cassettes to insure thin sectioning through the thickness of the each surgical mesh implant. The tissue strips were RT fixed in 10% formalin and processed using standard techniques of wax embedding, sectioning and H&E staining.

For qualitative analysis of each surgical mesh implant slide, standard light microscopic technique using a scoring system of 0 to 5 (0=none, 1=minimal, 2=mild, 3=moderate, 4=marked and 5=severe) for grading granulomatous inflammation, foreign body giant cell infiltrate, heterophil infiltrate, lymphocyte infiltrate, adipocyte infiltrate and fibrosis was used with attention paid to the consistency of response across the identified intramesh plane. For quantitative analysis, each surgical mesh implant slide was scanned and converted into high resolution digital image, with a base resolution of 0.5µm/pixel, at a scanning magnification of 20x. Prior to analysis, the sections were manually examined for birefringence under a standard microscope with a polarization filter as shown in Figure 2. The luminous expression of biomaterials facilitated clear identification of the plane of each mesh implant site. By using birefringence, observational bias in the identification of the track of the mesh plane for analysis was removed.

For the quantitative analysis to evaluate the continuity of fibrous connective tissue response, the mesh area was examined by systematically placing three measurement lines through the cross sectional plane of the mesh [20]. The midline, referenced hereafter as the “50” line (0 = vertical wound bed, 100 = vertical wound ceiling), is continuous from the beginning of one side of the mesh to the other. Because of the non-linearity of the mesh specimens, the midline was many times broken into continuous segments, creating angles that followed the course of the thickness of the surgical mesh. Upon completion of midline, two more parallel lines are measured in the outer periphery of the mesh, specifically at 10 and 90 percent of the thickness of the mesh segment, following the same angular pathways as the 50 line. Variability of the mesh thickness required the use of a least squares fitting measurement scheme, whereby groups of measurement lines can have different distances from the 50 lines than other groups. The terminal ends of the surgical mesh material exhibited variability and the measurement lines did not all end at the same point if the material did not itself as detailed in Figure 3.

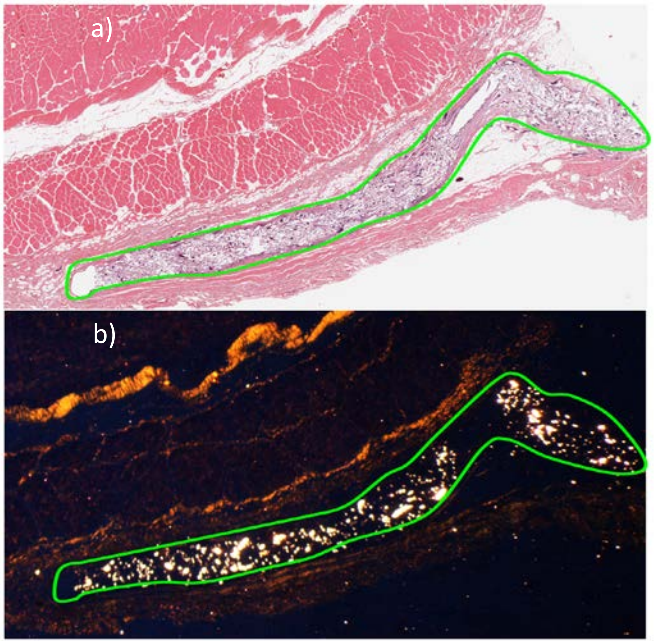


Figure 2: 1x image of NW PP under brightfield (a) and polarization (b), displaying green outline of area for analysis.

The 10-50-90 measurement lines were used as the sampling framework by which all normal healed tissue incorporation, adipose tissue and cutting artifact or mesh fiber (white space) lengths were measured. All 10-50-90 primary lines were assigned a green color and each individual line segment assigned a unique ascending number starting from 1 allowing data analysis per line segment - Figures 3a), 3b). The difference between the green line length (total) and the red (no response/mesh fiber) & yellow (fatty tissue) would be considered the normal healed tissue ingrowth composed primarily of fibrous connective tissue and granulomatous inflammatory response based upon the qualitative evaluation of the surgical mesh samples. The overlaid line segments spanned only the length the pathological feature of interest as shown in Figure 3.

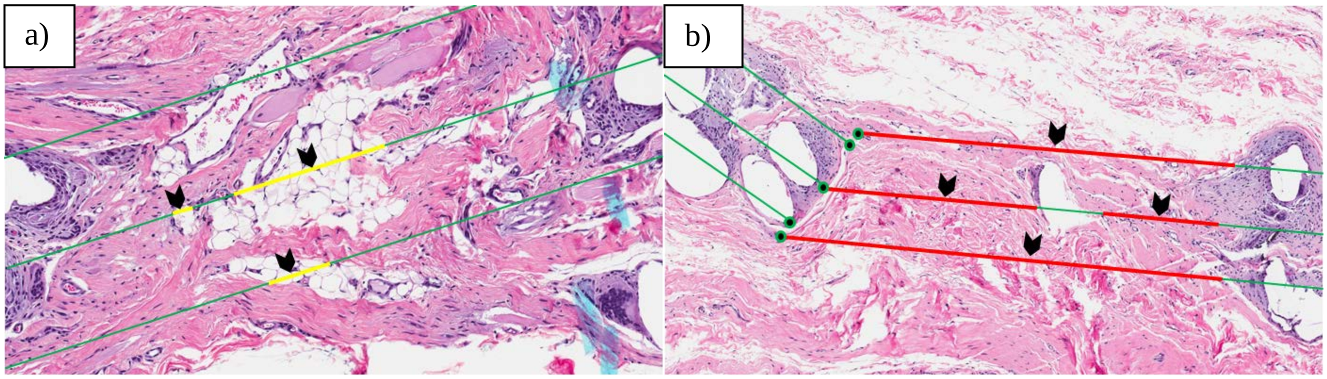


Figure 3: (a) H&E image displaying the 10-50-90 wound length measurement lines (green) and its overlaid fatty infiltrate (yellow) measurement at 15x. (b) H&E image at 10x displaying similar overlaid measurement lines but for no response tissue (red).

2.3 Modeling Approach and Statistical Analysis

The proportion of various types of tissue response served as the basis for comparing different types and constructions of surgical mesh. The outcome variable was defined as the proportion of each linear healed mesh measurement that corresponds to fatty tissue only (yellow) vs. the proportion that corresponds to normal tissue ingrowth (green length – red length) in determining the percentage of adipose tissue to fibrous connective/granulomatous tissue. For the purposes of this analysis, responses were categorized as a binary variable. Portions of each line corresponding to normal tissue ingrowth response represented a positive outcome, whereas portions corresponding to fatty tissue represented a negative outcome. Portions of tissue that were categorized as "no tissue response" were treated as missing data.

A univariate model was first fit with mesh type and construction as the only predictor variables [21]. Other covariates (vertical line position and quadrant) were tested individually but none were significantly associated with the outcome. Logistic regression was used to model the proportion of tissue response as a function of mesh type and construction as described earlier in Table 1. A generalized estimating equations (GEE) approach with robust variance estimation was used to account for the correlation among outcomes along the same line. The univariate model was chosen as the most appropriate analysis approach as shown in Table 2.

Table 2: Variable selection for logistic regression GEE models.

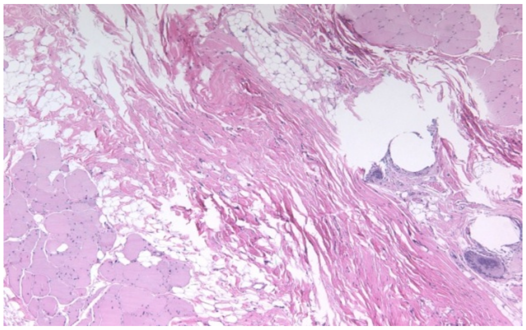
Model	QICu†	Variable	Score Test Statistic	P-value
Univariate*	18.45	Mesh Type	56.17	<0.0001
Adjusted, Vertical Line Position	20.56	Mesh Type	56.22	<0.0001
		10-50-90 Line	0.06	0.81
Adjusted , Quadrant	24.45	Mesh Type	44.42	<0.0001
		Quadrant	3.57	0.31
†QICu = Quasilikelihood, a statistic for comparing GEE models (model with smaller QICu is preferred).				

3. Results

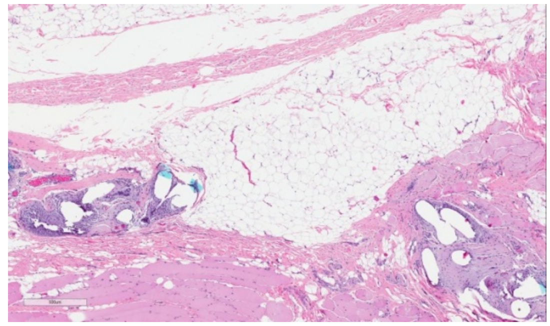
3.1 Qualitative Histopathology:

Sections of each surgical mesh implant type at 180 days were evaluated qualitatively to assess the overall tissue incorporation process morphology and analyzed quantitatively for fibrous connective tissue and adipose tissue presence within the plane of the surgical mesh. These endpoints are important as a fully or 100% fibrous connective tissue incorporated surgical mesh would yield a stronger hernia defect repair. Both qualitative and quantitative analyses focused on the plane of the surgical mesh as identified by the presence of mesh fibers, often following a non-linear path.

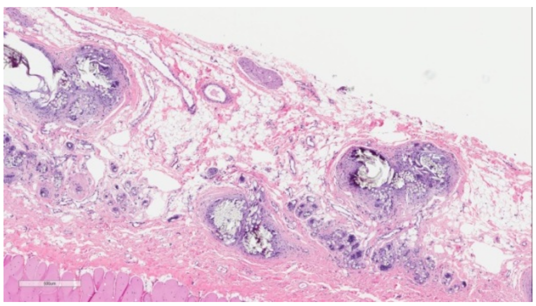
The general pattern of tissue incorporation to all knitted meshes was concentric in nature with a subsiding granulomatous inflammatory response and fibrosis located immediately adjacent to individual mesh fibers. In non-woven configurations, a planar zone of subsiding granulomatous inflammatory response and fibrosis throughout the intramesh area was found. These responses are shown in Figure 6 a-d. The specifics of the extent and character of the response to the different surgical mesh constructions varied greatly which are described below. Since the overall tissue response to each of the types of non-barrier and barrier surgical mesh constructions were similar at 180 days, the non-barrier mesh descriptions given below apply to both the non-barrier and barrier surgical mesh constructions.



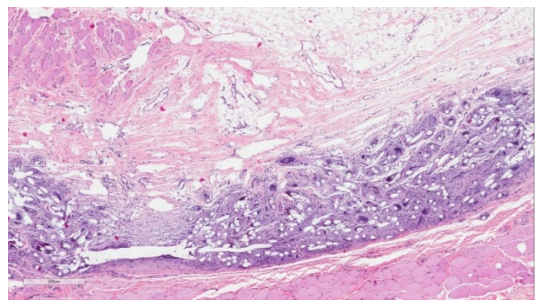
a) HW Knitted PP @ 4x



b) LW Knitted PP @ 4x



c) HW Knitted PET @ 4x



d) MW NW PP @ 4x

Figure 6: 4x overview of a) HW Knitted PP, b) LW Knitted PP, c) HW Knitted PET and d) MW NW PP demonstrating intramesh fibrous connective tissue formations in concentric (knitted constructions) versus laminar (non-woven) morphologies.

In LW PP knitted surgical mesh, minimal to mild granulomatous inflammation and fibrous connective tissue were consistently seen around groupings of mesh fibers but many times lacking between the groupings of fibers. Increased adipose tissue between the mesh fiber groupings was pronounced across sections of the LW PP knitted constructions, presenting discontinuities in the fibrous connective tissue response across the breadth of the mesh. In HW PP knitted mesh minimal granulomatous inflammation and mild numbers of foreign body giant cells were present, again concentrated around the mesh fibers. Fibrosis was observed focused around mesh fibers which at times led to a discontinuous response overall and one that was accompanied by mild amounts of adipose tissue infiltration between fiber groups.

In tissue cross-sections, HW PET knitted surgical mesh a mild to moderate granulomatous inflammation enveloped each individual fiber bundle, but did not always envelope every individual fiber comprising a bundle. As a result, empty cystic spaces were present in the central portion of most bundles. A sheath of moderate fibrosis surrounded the fiber bundles. The tissue response was not continuous, with gaps between clustered bundles of fibers that sometimes were occupied by a mild to moderate infiltrate of adipose tissue.

Mid-weight NW PP had a mild granulomatous inflammation and moderate amounts of fibrosis completely surrounding the mesh fibers leaving a smooth continuous layer of tissue response throughout the mesh. Mild numbers of foreign body giant cells and minimal numbers of heterophils and plasma cells were observed adjacent to the mesh fibers. The continuity of tissue response throughout the mesh excluded the presence of interposing adipocyte infiltration.

3.2 Quantitative Histopathology

With the use of birefringence, the sometimes tortuous path of the explanted mesh sections analyzed in this study was easily tracked. By mesh construction, the results between samples were very consistent with variances ranging from 0.1% for all non-woven constructions to 3.7% for all knitted constructions. For mesh type, the results between samples were similarly very consistent with variances ranging from 2.0% for all barrier mesh types to 3.8% for all non-barrier mesh types.

Disruptions in the ***non-barrier intramesh*** fibrous connective tissue at 180 days ranged from 0.2% (MW NW PP) to 18.9% (LW KN PP I) on average. The greatest percentage disruption in any given sample was 92.5% (LW KN PP II) with the minimum being 0.0% for all non-barrier surgical meshes analyzed. The average occurrence or frequency of disruptions in intramesh fibrous connective tissue ranged from 69.7% (HW KN PP) to 4.5% (MW NW PP) with all knitted non-barrier configurations averaging 51.0% +/- 13.2%.

Disruptions in the ***barrier intramesh*** fibrous connective tissue at 180 days ranged from 8.0% (MW KN PP/Omega 3 or ORC barrier) to 1.4% (MW NW PP/silicone) on average. The greatest percentage disruption in any given sample was 67.9% (MW KN PP/ORC) with the minimum being 0.0% for all barrier surgical meshes analyzed. The average occurrence or frequency of disruptions in intramesh fibrous connective tissue ranged from 38.5% (HW KN PET/collagen gel) to 8.0% (MW NW PP/silicone) with all knitted barrier configurations averaging 34.8% +/- 4.7%. Table 3 summarizes the results.

Table 3: Average rate, maximum rate and average occurrence of adipose tissue response at 180 days into knitted and non-woven surgical mesh configurations.

Surgical Mesh Category	N	Ave Adipose Tissue Response	Max Adipose Tissue Response	Ave Occurrence Adipose Tissue Response
Non-barrier Mesh				
LW KN PP I	75	18.9%	84.2%	50.7%
LW KN PP II	55	10.9%	92.5%	40.0%
HW KN PP	33	13.0%	49.5%	69.7%
HW KN PET	55	8.0%	57.8%	43.6%
WM NW PP	66	0.2%	13.8%	4.5%
Barrier Mesh [a]				
MW KN PP/Omega 3	66	8.0%	62.7%	36.4%
MW KN PP/ORC	105	8.0%	67.9%	29.5%
HW KN PET/collagen	39	6.4%	58.5%	38.5%
MW NW PP/silicone	87	1.4%	28.1%	8.0%
Mesh Type				
Non-barrier mesh	284	10.3%	13.8% - 92.5%	4.5% - 68.7%
Barrier Mesh	297	5.9%	28.1% - 67.9%	8.0% - 38.5%
Mesh Construction				
Knitted - KN	428	10.6%	49.5% - 92.5%	29.5% - 69.7%
Non-woven - NW	153	1.0%	13.8% - 28.1%	4.5% - 8.0%
[a] Non-barrier mesh base construction/barrier material				

Mesh type was significantly associated with differences in the overall distribution of fibrous connective and adipose tissues including the average percentage of fibrous connective tissue disruptions within a surgical mesh (Table 4, p-value<0.0001). The unadjusted proportions of fibrous connective tissue response and adipose tissue infiltrate for each type of mesh are listed in Table 3. MW NW PP had the highest proportion of fibrous connective tissue response (99.5%), while LW Knitted PP I had the lowest (82.9%) on average. The odds of a favorable fibrous connective tissue response were highest for MW NW PP. The odds ratio for MW NW PP compared to LW PP I was 37.6 times (Table 4, p-value<0.0001) indicating that the odds of fibrous connective tissue response exclusively are 37 times greater for MW NW PP than for LW PP I. There was also a significant difference between mesh technologies, where a non-woven mesh type had significantly higher odds of a fibrous connective tissue response than a knitted mesh type (OR=10.9, p-value<0.0001). Barrier meshes of all types had higher odds of a fibrous connective tissue response than non-barrier types overall, however, this difference was not statistically significant (OR=1.27, p-value=0.26). Estimated probabilities for fibrous connective tissue response and adipose response are provided along with 95% confidence intervals based on the GEE model in Table 4. These values are displayed graphically in Figure 7.

Table 4. Estimated probabilities and 95% confidence intervals for intramesh fibrous connective tissue and adipose tissue responses

	FC Tissue Response			Adipose Tissue Response		
Surgical Mesh Category	**Predicted Probability**	**Lower 95% Confidence Limit**	**Upper 95% Confidence Limit**	**Predicted Probability**	**Lower 95% Confidence Limit**	**Upper 95% Confidence Limit**
Mesh Type						
Non-barrier Mesh						
HW KN PP	88.6%	82.0%	93.0%	11.4%	7.0%	18.0%
LW KN PP I	82.9%	75.4%	88.5%	17.1%	11.5%	24.6%
LW KN PP II	88.8%	81.5%	93.4%	11.2%	6.6%	18.5%
HW KN PET	90.9%	86.3%	94.0%	9.1%	6.0%	13.7%
MW NW PP	99.5%	98.4%	99.8%	0.5%	0.2%	1.6%

Barrier Mesh						
MW KN PP/Omega 3 Gel	92.6%	88.9%	95.1%	7.5%	4.9%	11.1%
HW KN PET/collagen gel	93.8%	90.4%	96.0%	6.2%	4.0%	9.6%
MW KN PP/ORC	90.7%	86.4%	93.7%	9.3%	6.3%	13.6%
MW NW PP/silicone	98.2%	95.9%	99.2%	1.8%	0.8%	4.1%
Mesh Type						
Non-barrier	91.0%	88.6%	93.0%	9.0%	7.0%	11.4%
Barrier	93.6%	91.9%	94.9%	6.4%	5.1%	8.1%
Mesh Technology						
Knitted - KN	90.3%	88.6%	91.9%	9.7%	8.1%	11.4%
Non-Woven - NW	98.9%	97.7%	99.4%	1.1%	0.6%	2.3%

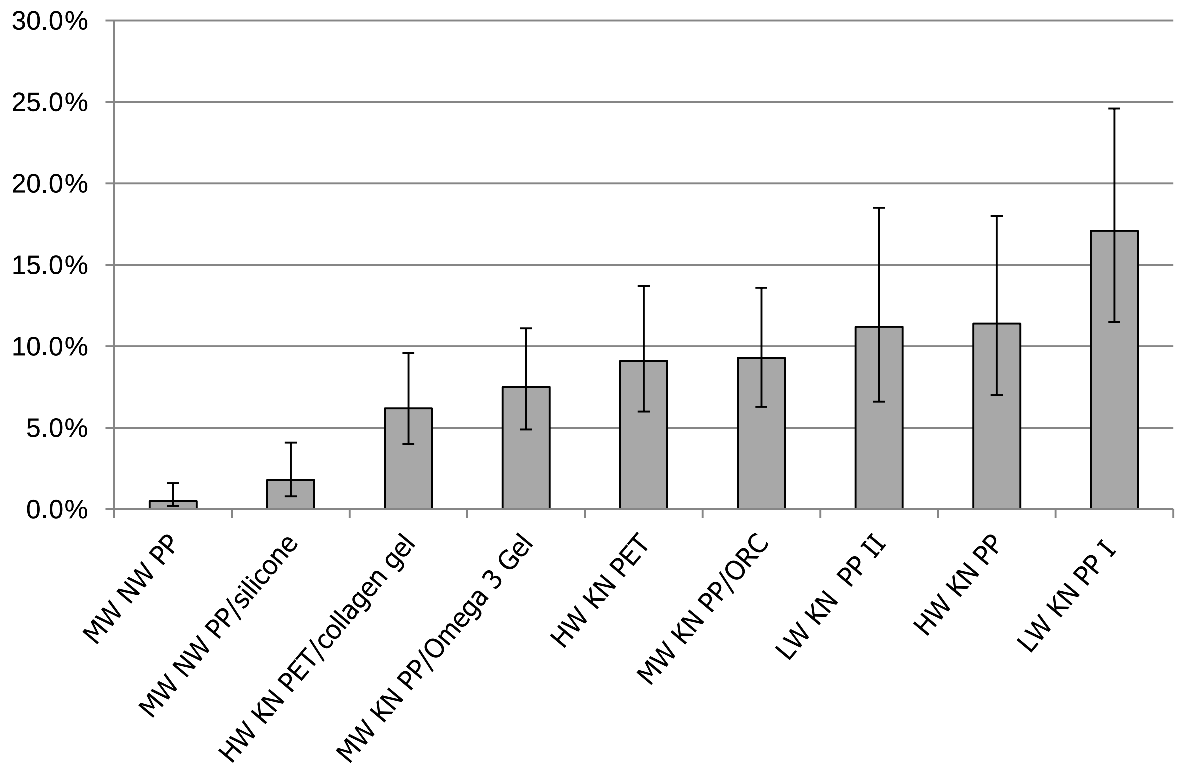


Figure 7: Estimated probability of fatty infiltrate with 95% confidence intervals by mesh type and construction

4. Discussion

Great strides have been made in the reconstruction of abdominal wall defects of all types through the refinement of surgical approaches and the increased use of advanced surgical mesh devices to reinforce abdominal wall tissues. Despite these advancements, recurrence rates, especially for ventral hernia repairs, persist. More recently, central mesh failures associated primarily with lighter weight surgical meshes have been reported [16-18, 22]. In considering the mechanics and pathophysiology of the abdominal wall hernia, a surgical mesh that results in the formation of a confluent layer of fibrous connective tissue across the mesh oriented along lines of tension in the abdominal wall and with no discontinuity in formed collagen or fibrous connective tissue, should come the closest to providing the strongest, healed reinforcement of an abdominal wall hernia defect.

Numerous published studies have observed the circumferential formation of fibrous connective tissue around knitted surgical mesh fibers (0.1 mm to 0.34 mm diameter) and their crossover connection points [23, 24], which was also confirmed in this study. This orientation of fibrous connective tissue in HW knitted constructions may be less problematic mechanically as the fibrous connective tissue granulomas are many times close enough together that a relatively consistent plane of interconnected and circumferentially oriented fibrous connective tissue is formed [23]. In LW knitted constructions, as the mesh fibers are separated by greater distances (1 to 4 mm), this circumferential orientation of fibrous connective tissue and collagen becomes more problematic by leading to discontinuities between adjacent mesh fibers and fiber junctions. These discontinuities would decrease the mechanical integrity of the formed fibrous connective tissue in the plane of the LW knitted surgical mesh across a hernia defect and introduce areas of stress concentration that could lead to introduction of a mechanical failure mode.

Conversely, in a non-woven surgical mesh configuration, especially one where very small (0.02 mm diameter) randomly oriented fibers are laid in a plane to form the surgical mesh, the developed fibrous connective tissue takes on a more planar morphology as the connective tissue follows the course of the mesh fibers. It has been determined previously that as long as the interconnecting spaces of a porous material are >75 microns [25, 26], fibroplasia, angiogenesis and collagen formation will occur. This was supported by the qualitative and quantitative histopathology results found with MW NW PP in this study. With the planar deposition of fibrous connective tissue, the healing intramesh spaces lead to the formation of collagen primarily oriented in the plane of the surgical mesh. With no or minimal disruptions in the healed fibrous connective tissue and collagen, such a surgical mesh would be much less likely to suffer stress concentrations that could lead to the development of a mechanical failure mode.

In this study histopathologic analysis of the plane of the surgical meshes both qualitatively and quantitatively after 180 days implantation demonstrated key differences in the morphology of wound healing between the knitted and non-woven configurations related to their physical construction. Discontinuities in the fibrous connective tissue of the healed barrier and non-barrier knitted meshes were common, with areas of adipose tissue deposition interrupting the continuity of the formed fibrous connective tissue. The discontinuities on average ranged from 7.5% for knitted barrier surgical meshes to 12.7% for knitted non-barrier surgical meshes with LW configurations exhibiting greater degrees of discontinuity. This difference between knitted non-barrier and barrier surgical meshes was not statistically significant in this implant model.

The non-woven type of surgical mesh used in this study resulted in significantly less fibrous connective tissue discontinuity of 0.5% for non-barrier and 1.4% for barrier configurations on average. This was found to be statistically ($p<0.0001$) less than that found with all knitted type surgical mesh configurations. In addition, through qualitative histopathology, the orientation of fibrous connective in knitted configurations tended to be more circumferential around mesh fibers whereas in non-woven samples it tended to be oriented with the plane of the mesh. As a surgical mesh in hernia repair is commonly oriented with fascial planes of tension, this planar fibrous connective tissue orientation has advantages in more consistently reinforcing repair sites. With the low probability for fibrous connective tissue discontinuities and the more planar orientation of formed fibrous connective tissue, a non-woven type structure would seem a better approach in designing surgical meshes to provide more consistent hernia defect reinforcement and prevent the development of mechanical failure modes.

The source of discontinuities in the healing fibrous connective tissue was the presence of adipose tissue. The source of the adipose tissue can be speculated to come from wound closure at the end of the initial surgical procedure or the presence of void space post operatively which fills with adipocytes. Numerous published experimental [24, 27] and clinical [5, 28] series on surgical meshes have commented on the presence of adipose tissue in the healing of surgical mesh inter-fiber void space. Until now the effect of the presence of adipose tissue around and between mesh fibers has not been discussed. This study, being performed in a relatively lean animal model, would be expected to be very conservative relative to the everyday clinical hernia repair on obese and morbidly obese patients. These results suggest that the occurrence of mid mesh mechanical failures can be expected in knitted surgical mesh constructions, especially LW configurations used in bridging type repairs. Additionally, in published clinical series on hernia repair [29] and of hernia mesh explants [5, 6, 30], recurrence remains one of the primary reasons for mesh explant and hernia revision. Definitive reasons are not yet available explaining this persistence of recurrence but it would be difficult to ignore incomplete fibrous connective tissue healing in intramesh spaces as a potential contributor to the persistence of recurrence.

In addition, adipose tissue and the individual fat cells, adipocytes, have been found to produce inflammation [31-34]. Most of the work on adipocytes has been in the context of obesity and diabetes. However, the same pro-inflammatory cells that produce inflammation in obesity, such as macrophages, have been proposed to be a mechanism for hernia mesh degradation [35]. Through materials characterization of explanted hernia meshes; surface chemical alterations, mass loss, physical alterations, surface cracking, fissuring and other deformities have been demonstrated. One potential mechanism for the physical and chemical alterations of hernia mesh in the body could be through an oxidation reaction by oxidants released from pro-inflammatory cells. There could be a higher risk this oxidation reaction around fat cells as compared to fibrous connective tissue cells.

5. Conclusion

In this comparative experimental evaluation, MW NW PP demonstrated significant improvement in the continuity of intramesh fibrous connective tissue and resistance to the presence of intramesh adipose tissue accumulations. With the increasing number of published clinical reports of central mesh failure, the presence of fibrous connective tissue discontinuities in healing knitted surgical mesh configurations, especially LW knitted configurations, suggests that the use of a surgical mesh configuration that does not result in fibrous tissue discontinuities should be considered. The significant reduction in formed fibrous connective tissue discontinuities with MW NW PP seems related to the random and planar distribution of very small mesh fibers throughout the non-woven mesh that creates a structure which precludes the physical penetration of adipose tissue yet supports the formation of fibrous connective tissue. Using a surgical mesh which maximizes the continuity of formed fibrous connective tissue throughout the mesh structure should only help reduce the ongoing problem of hernia recurrence and potentially eliminate problems with central mesh failure in abdominal wall defect repairs. An ongoing clinical quality improvement project measuring the long term outcomes of patients undergoing ventral hernia repair using MW NW PP/silicone barrier mesh will help to define the potential for recurrence reduction and improved patient outcomes when using a non-woven type of surgical mesh routinely.

Acknowledgements

The authors gratefully acknowledge the efforts and excellence of the staff and director of the Surgical Research Laboratory at Dartmouth Hitchcock Medical Center and Dartmouth College.

Funding for the rabbit implant study and histopathologic analysis was provided by BG Medical, LLC.

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